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Mucoadhesive Drug Delivery Systems: Formulation and Dosage form Aspects

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Abstract **Review Article**

Mucoadhesive drug delivery systems (MDDS) represent an innovative in the design of drug delivery systems, and represent an innovative method for administering drugs through oral routes such as the buccal, sublingual, and gingival areas. These systems leverage natural or synthetic polymers to ensure prolonged adherence to mucosal surfaces, enabling extended and controlled release of medication. Several factors influence the effectiveness of mucoadhesion, including the hydrophilicity of polymers, molecular weight, and environmental factors like pH and moisture levels. MDDS can take various forms, including tablets, films, patches, powder, ointments and gels, each offering different drug release profiles such as immediate, sustained, or controlled. These systems enhance drug bioavailability by avoiding first-pass metabolism, making them particularly beneficial for medications with low oral bioavailability or those requiring targeted delivery. Although MDDS offer improved patient compliance and therapeutic effectiveness, they still face challenges like irritation, taste concerns, and the diluting effect of saliva, which can impact drug stability. Despite these challenges, MDDS hold significant promise for advancing drug delivery technologies across various medical applications. This review thoroughly examines the mechanisms, theories of bioadhesion, advantages, routes of administration, and dosage forms of mucoadhesive drug delivery systems.

Keywords: Mucoadhesive, Drug delivery systems, Therapeutic, Polymers, Sustained, Bioavailability, Tablets.

INTRODUCTION

The concept of mucoadhesion was introduced in the field of controlled release drug delivery systems in the early 1980s [1,2]. Thereafter, several researchers have focused on the investigations of the interfacial phenomena of mucoadhesive hydro gels with the mucus. For drug delivery purpose, the term bioadhesion implies attachment of a drug carrier system to a specific biological location. The development of NDDS has been made possible by the various compatible polymers to modify the release pattern of drug. In the recent years the interest is growing to develop a drug delivery system with the use of a mucoadhesive polymer that will attach to related tissue or to the surface coating of the tissue for the targeting various absorptive mucosa such as ocular, nasal, pulmonary, buccal, vaginal etc. This system of drug delivery is called as mucoadhesive drug delivery system.

Mucoadhesive polymers are synthetic or natural macromolecules which are capable of attaching to mucosal surfaces. The concept of mucoadhesive polymers has been introduced into the pharmaceutical literature more than 40 years ago and nowadays it has been accepted as a promising strategy to prolong the residence time and to improve the specific localization of drug delivery systems on various membranes. Amongst the various routes of drug delivery, oral route is perhaps the most preferred to the patient and the clinician alike. However, per oral administration of drugs has disadvantages such as hepatic first pass metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain classes of drugs especially peptides and proteins. Consequently, other absorptive mucosae are considered as potential sites for drug administration. The oral mucosa has many properties which make it an attractive site for drug delivery but also provides several challenges for researchers investigating novel delivery techniques to overcome many different formulations including sprays, tablets, mouthwashes, gels, pastes and patches are presently used for delivery into and/ or across the oral mucosa [3, 4]. The term bioadhesion refers to any bond formed between two

biological surfaces or a bond between a biological and a synthetic surface. In case of bioadhesive drug delivery, the term bioadhesion is used to describe the adhesion between polymers, either synthetic or natural and soft tissues or the gastrointestinal mucosa. In cases where the bond is formed with the mucus the term mucoadhesion may be used synonymously with bioadhesion. Bioadhesion can be defined as a phenomenon of interfacial molecular attractive forces in the midst of the surfaces of the biological substrate and the natural or synthetic polymers, which allows the polymer to adhere to the biological surface for an extended period of time [5-8]. Bioadhesive polymeric systems have been used since extent in the development of products for various biomedical applications which include denture adhesives and surgical glue [9-12]. The adhesion of bacteria to the human gut may be attributed to the interaction of lectin-like structure (present on the cell surface of bacteria) and mucin (present in the biological tissues) [13-16]. Various biopolymers show the bioadhesive properties and have been utilized for various therapeutic purposes in medicine [6]. Mucoadhesive drug delivery systems are delivery systems which utilized the assets of bioadhesion of certain polymers which become adhesive on hydration and thus can be used for targeting a drug to exacting region of the body for extended period of time [5].

Pharmaceutical aspects of mucoadhesion have been the subject of great significance during recent years because it provides the chance of avoiding either destruction by gastrointestinal contents or hepatic first-pass inactivation of drug.

Mucoadhesive formulation contains one or more hydrophilic polymers along with drug. When it comes in contact to saliva, due to the aqueous nature of saliva it becomes wet and the drug releases from the system. Simultaneously modified drug delivery system (MDDS) adheres to the mucous with some physical interaction. Mucous, secreted from salivary gland or epithelial glands is an aqueous based viscoelastic complex mixture of proteins, nucleic acid, immunoglobulins, enzymes, lipids and several ionic species [17]. Functionally mucus membrane or mucosa provides a protective barrier, an adhesive function and lubricant effect [18]. The success of MDDS depends on the ability of the polymer/s to retain at the mucous layer and to sustain the drug release. This indicates the importance of polymeric properties for successful development of mucoadhesive preparation.

MUCOADHESIVE DRUG DELIVERY SYSTEM

The mucus layer that covers the mucosal epithelial surface of the body is intended to interact with a mucoadhesive medication delivery device. Mucin molecules, which are specific glycoproteins, are found in the mucus layer. Due to particular chemical interactions between the mucoadhesive agents and the mucin molecules, the mucoadhesive dosage form clings to the mucus layer when applied or delivered. This adhesion increases the drug system's resident time at the absorption site by allowing it to stay in close contact with the mucosal surface. The lengthening of the stay gives the medication additional chances to cross the mucosal barrier and enter the bloodstream. This procedure can increase the effectiveness of drug administration, which may result in improved therapeutic outcomes with less frequent doses and fewer side effects. A promising method for localized drug administration in a variety of medical applications, such as the treatment of oral, nasal, ophthalmic, or vaginal disorders, is the mucoadhesive drug system's capacity to attach to the mucosal surface and prolong residence time [19].

A mucoadhesive drug delivery system is a specific method that improves the effects of drugs by extending the period of time in which they are in touch with the targeted mucosal surface. This system is made to stick to mucous membranes, like those in the nasal passages, over time, there has been a notable transition in pharmaceutical research focus. Previously, the main emphasis was on creating new chemical entities for drugs. However, this emphasis has shifted towards a more innovative approach known as Novel Drug Delivery System (NDDS). This new approach involves enhancing the effectiveness of existing drug molecules by developing advanced methods of delivering them into the body. The goal is to optimize their therapeutic action while ensuring patient safety and protection. This shift in research direction promises to revolutionize drug development and healthcare outcomes [20]. Over time, there has been a notable transition in pharmaceutical research focus. Previously, the main emphasis was on creating new chemical entities for drugs. However, this emphasis has shifted towards a more innovative approach known as Novel Drug Delivery System (NDDS). This new approach involves enhancing the effectiveness of existing drug molecules by developing advanced methods of delivering them into the body. The goal is to optimize their therapeutic action while ensuring patient safety and protection. This shift in research direction promises to revolutionize drug development and healthcare outcomes. Pharmaceutical research has undergone a noticeable shift in focus over time. Prior to now, developing novel chemical entities for medications was the main focus. However, the focus now lies on a novel strategy called as Novel Drug Delivery System (NDDS). This novel strategy entails improving the potency of currently available pharmacological compounds by creating cutting-edge delivery systems. The objective is to maximize their therapeutic effect while assuring the security and protection of the patient. This change in research focus has the potential to completely transform drug development and healthcare outcomes [21]. Mucoadhesive drug transport systems are a type of bioadhesive drug administration technology. These solutions take advantage of the particular property of specific polymers that exhibit adhesiveness during hydration. This property allows them to stick effectively to mucosal surfaces, allowing for precise drug

concentration in a specific body location for extended periods of time [22]. Sustained-release dosage forms are designed to gradually release the active substance over time, but sometimes, this gradual release may not be enough to ensure a therapeutic effect. In some cases, these dosage forms can be prematurely removed from the absorption site before all the medication has been released. On the other hand, mucoadhesive dosage forms are designed to address this issue by helping to maintain a controlled release of the medication at the site of absorption.

Over the years, various mucoadhesive drug delivery methods have been developed to achieve both local and systemic effects, administered through routes such as nasal, buccal, oral, vaginal, and rectal administration [23].

Mechanism and Theory of Bioadhesion

The mechanisms by which mucoadhesive bonds form are not completely clear. It is generally accepted that the process involves three steps [24]: Wetting and swelling of polymer to permit intimate contact with biological tissue, interpenetration of bioadhesive polymer chains with mucin molecules leading to entanglement and formation of weak chemical bonds between entangled chains. Five theories of adhesion have been developed to explain the properties of a wide range of materials including glues, adhesives and paint [25]:

i. The electronic theory assumes that the different electronic structures of the mucoadhesive and the biological material result in electron transfer upon contact.
ii. The adsorption theory states that the bioadhesive bond is due to van der Waals interactions and hydrogen bonds. This is the most widely accepted theory of adhesion. (iii) The wetting theory uses interfacial tension to predict the degree of spreading of, for example, a gel formulation on the mucosa, which can then be used to predict the degree of mucoadhesion.
iii. The diffusion theory states that interpenetration and entanglement of polymer chains are responsible for mucoadhesion. The more structurally similar a mucoadhesive is to the mucosa, the greater the mucoadhesion will be. It is believed that an interpenetration layer of 0.2-0.5 m is required to produce an effective bond.
iv. The fracture theory analyzes the force required to separate two surfaces after adhesion. It is often used for calculating fracture strengths of adhesive bonds during detachment.

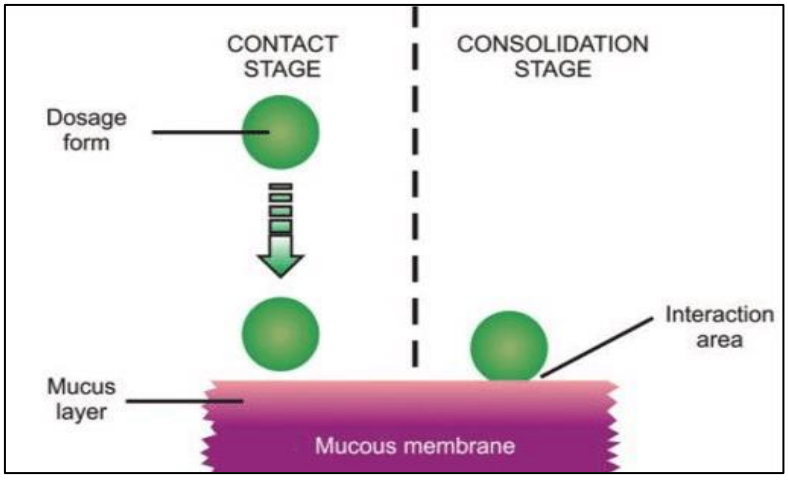

Figure 1: Mechanism of mucoadhesion

Factors Affecting to Mucoadhesion

Polymer based factors

Molecular weight of polymer

As the molecular weight of polymer is low, it can penetrate better in the mucus. The molecular weight can increases with increase in molecular weight up to 10,000above that the mucoadhesive strength decreases. For linear polymer the bioadhesiveness improve with increase in molecular weight which depends on two things that for lower molecular weight, interpenetration is more critical and entanglement is important for higher molecular weight [26].

CONCENTRATION OF POLYMER

This factor depends on type of dosage form. In case of solid dosage form, the higher the concentration of polymer, the stronger the mucoadhesion. However, for liquid dosage form, maximum mucoadhesion is shown when there is an optimum polymer concentration [27].

MUCOADHESION THEORIES

Various theories exist to explain at least some of the experimental observations made during the bioadhesion process. Unfortunately, each theoretical model can only explain a limited number of the diverse

range of interactions that constitute the bioadhesive bond [28]. However five main theories can be distinguish.
(a)Wetting theory
(b) Electronic theory
(c) Fracture theory
(d) Adsorption theory
(e) Diffusion theory

MUCOADHESIVE POLYMERS

A polymer is an intriguing substance or material made up of macromolecules, very big molecules. These macromolecules are known as polymers, which are characterized by a large number of repetitive components. Polymers are essential and ubiquitous in our daily lives due to the wide range of features they contain. Whether they are made artificially or naturally, polymers are made by a process known as polymerization in which numerous small molecules, or monomers, chemically bind together to create these large macromolecules [29, 30]. The combining of multiple smaller molecules, known as monomers, results in polymers, which are large molecules known as macromolecules. These smaller units undergo a conversion process to create the big, intricate structures that are unique to polymers. The Greek terms "poly" (which means "many") and "meros," which means "parts or members," are the source of the English word "polymer." It alludes to massive molecules made up of recurring monomeric building blocks. Natural polymers have been present on Earth since prehistoric times and are essential to life. They are polymers in a liquid or semi-solid state. Speaking of adhesives, they too are frequently crafted from polymers to produce gooey materials that bind surfaces together. Adhesive tapes, which combine polymers and adhesives, provide a practical way to attach objects [31]. Polymers are fascinating giant molecules with high molecular weight, known as macromolecules. They are formed through a process called polymerization, where numerous small molecules, called monomers, are intricately linked together. The physicochemical characteristics of the polymers employed in the formulation determine how well solid dosage forms, implants, dispersion systems, transdermal patches, and particle systems work. The sales of pharmaceutical polymers make up a very modest fraction of the total polymer market. The Food and Drug Administration closely monitors these polymers' standards to ensure that their use has no unfavorable impacts [32, 33].

CLASSIFICATION OF MUCOADHESIVE POLYMERS

Based on Origin

Synthetic mucoadhesive polymers:
Cellulose derivatives, Poly (acrylic acid) polymers, Poly (hydroxyethyl methylacrylate), Poly (ethylene oxide), Poly (vinyl pyrrolidone), Poly (vinyl alcohol).
Natural mucoadhesive polymers:
Tragacanth, Sodium alginate, Karaya gum, Guar gum, Xanthan gum, Soluble starch, Gelatin, Pectin, Chitosan, etc .

Based on Nature

Hydrophilic polymers:

The polymers within this category are soluble in water. Matrices developed with these polymers swell when put into an aqueous media with subsequent dissolution of the matrix. The polyelectrolytes extend greater mucoadhesive property. e.g. poloxamer, hydroxypropyl methyl cellulose, methyl cellulose, poly (vinyl alcohol) and poly (vinyl pyrrolidone), have also been used for mucoadhesive properties.

Polysaccharides and its derivatives:

Numerous polysaccharides and its derivatives like chitosan, methyl cellulose, hyaluronic acid, hydroxy propyl methylcellulose, hydroxy propyl cellulose, Xanthan gum, gellan gum, guar gum, and Carrageenan have found applications in ocular mucoadhesive delivery systems. Cellulose and its derivatives have been reported to have surface active property in addition to its film forming capability. Cellulose derivatives with lower surface acting property are generally preferred in ocular delivery systems as they cause reduced eye irritation. Of the various cellulose derivatives, sodium carboxymethyl cellulose has been found to have excellent ocular mucoadhesive property. Cationic cellulose derivatives (e.g. cationic hydroxyethyl celluloses) have been used in conjunction with various anionic polymers for the development of sustained delivery systems.

Hydrogels:

Hydrogels can be defined as three-dimensionally cross-linked polymer chains which have the ability to hold water within its porous structure. The water holding capacity of the hydrogels is mainly due to the presence of hydrophilic functional groups like hydroxyl, amino and carboxyl groups. In addition to the drug targeting, mucoadhesive hydrogel based formulations for improving the bioavailability of the poorly water soluble drug. This was attributed to the increased retention time of the delivery system within the gastrointestinal tract [34].

Factors affecting mucoadhesive drug delivery system

Polymer related factors:

Molecular weight:

The mucoadhesive strength of a polymer increases with molecular weights above 100,000. Direct correlation between the mucoadhesive strength of polyoxyethylene polymers and their molecular weights lies in the range of 200,000–7,000,000 [35].

Chain length:

With the increase in the chain length of the polymers there is an increase in the
mucoadhesive property of the polymer.

Spatial arrangement:

Spatial conformation of a molecule is also important factor. Besides molecular weight or chain length, spatial conformation of a molecule is also important. The helical conformation of dextran may shield many adhesively active groups primarily responsible for adhesion, unlike PEG polymers which have a linear confirmation. Mucoadhesion starts with the diffusion of the polymer chains in the interfacial region. Therefore, it is important that the polymer chains contain a substantial degree of flexibility in order to achieve the desired entanglement with the mucus [36]. The increased chain interpenetration was attributed to the increased structural flexibility of the polymer upon incorporation of polyethylene glycol. In general, mobility and flexibility of polymers can be related to their viscosities and diffusion coefficients, as higher flexibility of a polymer causes greater diffusion into the mucus network [37].

Cross-linking density:

The average pore size, the number and average molecular weight of the cross-linked polymers, and the density of cross-linking are three important and inter-related structural parameters of a polymer network. Therefore, it seems reasonable that with increasing density of crosslinking, diffusion of water into the polymer network occurs at a lower rate which, in turn, causes an insufficient swelling of the polymer and a decreased rate of interpenetration between polymer and mucin [37].

Hydrogen bonding capacity:

Hydrogen bonding is another important factor in mucoadhesion of a polymer. Desired polymers must have functional groups that are able to form hydrogen bonds, and flexibility of the polymer is important to improve this hydrogen bonding potential [37]. Polymers such as poly(vinyl alcohol), hydroxylated methacrylate, and poly(methacrylic acid), as well as all their copolymers, have good hydrogen bonding capacity [38].

Hydration:

Hydration is required for a mucoadhesive polymer to expand and create a proper macromolecular mes of sufficient size, and also to induce mobility in the polymer chains in order to enhance the interpenetration process between polymer and mucin. Polymer swelling permits a mechanical entanglement by exposing the bioadhesive sites for hydrogen bonding and/or electrostatic interaction between the polymer and the mucus network [37]. However, a critical degree of hydration of the mucoadhesive polymer exists where optimum swelling and mucoadhesion occurs [38].

Charge:

Some generalizations about the charge of bioadhesive polymers have been made previously, where nonionic polymers appear to undergo a smaller degree of adhesion compared to anionic polymers. Strong anionic charge on the polymer is one of the required characteristics for mucoadhesion [38]. Some cationic polymers are likely to demonstrate superior mucoadhesive properties, especially in a neutral or slightly alkaline medium [39]. Additionally, some cationic high–molecular-weight polymers, such as chitosan, have shown to possess good adhesive properties [40]. There is no significant literature about the influence of the charge of the membrane on the mucoadhesion but the pH of the membrane affects the mucoadhesion as it can influence the ionized or un-ionized forms of the polymers [41].

Concentration:

The importance of this factor lies in the development of a strong adhesive bond with the mucus, and can be explained by the polymer chain length available for penetration into the mucus layer. When the concentration of the polymer is too low, the number of penetrating polymer chains per

unit volume of the mucus is small and the interaction between polymer and mucus is unstable. In general, the more concentrated polymer would result in a longer penetrating chain length and better adhesion. However, for each polymer, there is a critical concentration, above which the polymer produces an “unperturbed” state due to a significantly coiled structure. As a result, the accessibility of the solvent to the polymer decreases, and chain penetration of the polymer is drastically reduced. Therefore, higher concentrations of polymers do not necessarily improve and, in some cases, actually diminish mucoadhesive properties. One of the studies addressing this factor demonstrated that high concentrations of flexible polymeric films based on polyvinylpyrrolidone or poly(vinyl alcohol) as film-forming polymers did not further enhance the mucoadhesive properties of the polymer [42].

Environmental factors

Apart from the above mentioned physicochemical properties of the polymeric network, various environmental factors also play an important role in mucoadhesion.

a. pH
b. Applied strength
c. Contact time
d. Swelling

Physiological factors

The physiological factors which play an important role in governing the mucoadhesive property of a polymer matrix include texture and thickness of mucosa.

(i) Mucin turnover (ii) Disease state

An ideal mucoadhesive polymer has the following characteristics [43, 44].

1. The polymer and its degradation products should be nontoxic and should be non- absorbable from the gastrointestinal tract.
2. It should be nonirritant to the mucous membrane.
3. It should preferably form a strong non-covalent bond with the mucin-epithelial cell surfaces.
4. It should adhere quickly to most tissue and should possess some site-specificity.
5. It should allow daily incorporation to the drug and offer no hindrance to its release.
6. The polymer must not decompose on storage or during the shelf life of the dosage form.
7. The cost of polymer should not be high so that the prepared dosage form remains competitive.

Ideal Characteristics of Buccal Adhesive Polymers: [45]

1) Polymer and its degradation products should be non-toxic, non-irritant and free from leachable impurities.
1) 2)Should have good spreadability, wetting, swelling and solubility and biodegradability properties.
2) Should adhere quickly to buccal mucosa and should possess sufficient mechanical strength.
3) Should possess peel, tensile and shear strengths at the bioadhesive range.
4) Polymer must be easily available and its cost should not be high.
5) Should show bioadhesive properties in both dry and liquid state.
6) Should demonstrate local enzyme inhibition and penetration enhancement properties.
7) Should demonstrate acceptable shelf life.
8) Should have optimum molecular weight.
9) Should possess adhesively active groups.
10) Should have required spatial conformation.
11) Should be sufficiently cross-linked but not to the degree of suppression of bond forming groups.
12) Should not aid in development of secondary infections such as dental caries.

Route of Mucoadhesive Drug Delivery System

Systems for mucoadhesive drug delivery prolong the time the dose form is left at the application site, improving absorption. For systemic and local effects via oral, buccal, nasal, rectal, and vaginal routes, various such systems have been created recently. The concept of mucoadhesion has garnered significant attention in the pharmaceutical field and is effectively employed as an administration method. Mucoadhesive drug delivery systems can be administered through various routes.

Buccal Delivery System:

An alternative to oral administration for medications affected by the first-pass effect is buccal drug delivery. Long regarded as an ideal location for medication administration, the stratified squamous epithelium in the buccal mucosa is supported by connective tissue lamina propria. Buccal administration has benefits including simple accessibility, epithelial resilience, flexible dose, and decreased vulnerability to enzymatic activity. As a result, oral administration systems for sticky mucosal dosage forms, including adhesive tablets, gels, and patches, have been created. The development of efficient bio adhesive buccal delivery methods, however, still faces a major issue with the absorption of hydrophilic medicines through the membrane.

Oral Delivery System:

The goal of a system created for oral drug administration is to provide consistent drug release as the patient's digestive system moves through it. Even while oral delivery is popular and well-liked by patients, it has challenges because of interactions with the gastrointestinal system and drug effectiveness. A lot of research has been done on lipid-based oral delivery systems, with a focus on how each system component affects delivery effectiveness and the route of lipid-based oral administration [46].

Vaginal Delivery System:

The uterus is connected to the outside of the body by the vagina, which acts as a fibrovascular conduit. Lamina propria and squamous epithelium are used to line it. There are many other dose forms that can be used for vaginal administration, including solutions, gels, suspensions, suppositories, creams, and tablets, although they usually only stay in the vagina for a short time. Bioadhesive compounds can extend the shelf life of vaginal formulations and control the rate of medication release. To treat vaginal dryness, these formulations may contain medication or even work in conjunction with moisturizers.

The potential of vaginal gels has been enhanced by recent advancements in polymer technology. A little amount of solid material is scattered inside a relatively larger volume of liquid to form these gels, which are semi-solid polymer structures. They have found use as microbicides, contraceptives, labor inducers, and other chemicals, among other things.

Rectal Delivery System:

A section of the colon called the rectum has a surface area of 300 cm2 and a length of around 10 cm. Its main function is to remove water. Its surface area for medication absorption is considerably constrained due to the lack of villi. The rectum primarily absorbs drugs through simple diffusion over the lipid membrane. Rectal administration offers significant benefits for substances that are prone to significant first-pass metabolism,

especially when administered to areas close to the anus. Additionally, it has been noted that the migration distance within the rectum is reduced by the addition of bioadhesive polymers [47]. Rectal drug delivery refers to the administration of pharmaceuticals through the rectum to produce effects either locally or systemically throughout the body. Rectal drug distribution is one method of medication administration that makes use of mucosal adhesion. These systems have mucoadhesive characteristics, which means that a strong carrier helps the medicine attach to the mucous membrane.

Nasal Delivery System:

Nasal administration, commonly referred to as snorting, is a method of delivering drugs by inhaling them through the nose. Furthermore, factors such as the nasal floor, drug concentration and amount, the physical state of the dosage form, and the positioning of the head during administration all contribute to the drug absorption process. This route of administration encompasses several applications:

1) Utilization of nasal tablets for local drug delivery
2) Achieving systemic drug delivery
3) Transporting drugs from the nose to the brain
4) Delivery of nasal vaccines.

Ocular Delivery System:

The eye is a sophisticated organ that has unique anatomical and physiological characteristics. A unique drug delivery technique includes injecting the medication into the ODDS, also known as the conjunctival cavity of the eye. A specialized, sterile method of creating dosage forms is called ophthalmic preparation. Drugs can be administered intravenously for intraocular therapies, topically for topical treatments, or next to the eye for periocular treatments. Pharmaceutical researchers and experts deal with one of the most fascinating and difficult parts of ODDS. Usually, ocular drugs are injected directly into the eye. Drug potency, bioavailability, and clearance at the targeted location are only a few examples of the variables that affect how effectively drugs are delivered in terms of drug loading, release rate, and retention time in the eye [46].

Gastrointestinal Delivery System:

The oral route is undoubtedly the most desired way of administration, but there are some serious risks with it, including hepatic first-pass metabolism, drug degradation during absorption, the presence of mucus on GI epithelia, and rapid mucus turnover. Delivery through the gastrointestinal tract (GIT) has been more well-known recently as a major administration route. Systems that use bio adhesive polymers to adhere to the epithelial surface in the GIT are called bio adhesive retentive systems. The use of bio adhesive polymers can prolong GI transit time and increase bioavailability [47].

Mucoadhesive Dosage Forms

Tablet:

Mucoadhesive tablets are typically oval-shaped, flat, and tiny, with a diameter of 5-8 mm. These tablets allow speaking and drinking without causing undue discomfort, in contrast to conventional tablets. When they soften, they cling to the mucous membranes and stay there until they break down or release their contents. Tablets that adhere to the mucous membrane may allow for controlled medication release. Tablets having mucoadhesive qualities provide a number of advantages, including enhanced mucus layer interaction and increased drug absorption and bioavailability due to a larger surface-to-volume ratio. Tablets that are mucoadhesive can be designed to adhere to different mucosal tissues, including those in the stomach, allowing for both targeted and more extensive controlled drug release. To achieve targeted pharmacological effects, these tablets are placed on the gastrointestinal mucosa. Due to their prolonged medication release, mucoadhesive tablets are well-liked because they reduce the need for frequent dosage and improve patient adherence. However, a noteworthy disadvantage of these pills is their lack of flexibility, which, when taken repeatedly or for a lengthy period of time, may diminish patient compliance.

Films:

Mucoadhesive films might be preferable over adhesive tablets due to their greater flexibility and comfort. They address the issue of oral gels having a short duration on mucosal surfaces since they aren't easily washed away by saliva. Additionally, when used for localized oral treatments, these films protect wounds, reducing pain and enhancing treatment effectiveness. An ideal film should be pliable, elastic, and soft while remaining sufficiently sturdy to endure the stresses of mouth movement. It's also important for the film to have strong adhesive properties to remain in the mouth for the necessary duration of action. Excessive swelling, if it does occur, should be avoided to prevent discomfort.

Patches:

An impermeable backing, a reservoir layer containing the medication for controlled release, and a mucoadhesive surface for adhering to mucosal tissue are the layers that make up patches. Similar patch delivery technologies are employed in transdermal medicine delivery. The processes of solvent casting and direct milling are both used to make adhesive patches. The solvent casting technique involves pouring a drug and polymer solution over a backing layer, which causes the solvent(s) to evaporate, creating an intermediate sheet. The formulation's components are combined, compacted to the correct thickness, and then cut or punched into predetermined patch forms in the direct milling process. To regulate drug release direction, avoid drug loss, and maintain device integrity while in operation, an impermeable backing layer can be applied.

Gel & Ointments:

The benefit of being simple to apply over the oral mucosa is provided by semi-solid formulations like gels and ointments. Their precise dose, however, could not be as precise as that of tablets, patches, or films. Mucoadhesive formulations are used to solve the problem of keeping gels at the application site. Some mucoadhesive polymers, like sodium carboxymethylcellulose, carpbapol, hyaluronic acid, and xanthan gum, go through a phase transition from liquid to semi-solid, enhancing viscosity for prolonged and controlled drug release. Additionally promising for buccal medication delivery are hydrogels. These gels are created from water-absorbing polymers that hold medication molecules when hydrated and release them gradually through diffusion or erosion.

The use of mucoadhesive gels offers benefits like prolonged retention in the mouth, effective drug penetration, and high patient satisfaction. A significant application of these gels is in locally delivering medications for treating periodontitis, an inflammatory and infectious gum disease leading to pockets between teeth and gums, often resulting in tooth loss. Mucoadhesive polymers integrated into antimicrobial formulations can be injected into periodontal pockets using a syringe, potentially aiding periodontitis therapy. Furthermore, a highly viscous gel composed of carpool and hydroxypropyl cellulose was created for ointment applications, maintaining tissue contact for up to 8 hours [48].

Powders:

Powder-based mucoadhesive formulations have gained significant traction in nasal drug delivery. In contrast to liquid counterparts, these formulations, which include both the medication and mucoadhesive components (often polymers), have demonstrated the ability to improve the bioavailability of drugs by extending their presence at the absorption or target site [49]. When powdered HPC and beclomethasone are sprayed onto the oral mucosa of rats, a significantly prolonged residence period is observed compared to using an oral solution. Furthermore, there is a notable 2.5% retention of beclomethasone on the buccal mucosa for a duration of up to 4 hours [49].

CONCLUSION

Mucoadhesive systems have become a potential approach in pharmaceutical technology for improving drug delivery. This overview about the mucoadhesive dosage forms might be a useful tool for the efficient design of novel mucoadhesive drug delivery systems. Mucoadhesive drug delivery systems have applications from different angles, including development of novel mucoadhesives, design of the device, mechanisms of mucoadhesion and permeation enhancement. With the influx of a large number of new drug molecules due to drug discovery, mucoadhesive drug delivery will play an even more important role in delivering these molecules. This novel method of drug delivery has enormous potential to revolutionize healthcare and improve treatment results.

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